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Case Records of the Massachusetts General Hospital

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

Case 37-2000

PRESENTATION OF CASE

An 11-day-old boy was admitted to the hospital because of an osteolytic lesion in the right tibia.

The infant was born at 39½ weeks' gestation to a woman who had had one previous pregnancy, which had ended in a spontaneous abortion. Her immunizations were up to date. She had attended all prenatal examinations and had taken prenatal vitamins. She had refused a test to measure the alpha-fetoprotein level and an amniocentesis. The results of all other routine prenatal laboratory tests were normal, and a vaginal culture for group B streptococci was negative. Vaginal delivery was induced because of mild hypertension and was uncomplicated. The mother had no history of fever or use of medications.

The infant's weight at birth was 3551 g. On initial examination, the infant winced and retracted his right leg when it was touched. A radiograph (Fig. 1), obtained on the day of birth, showed an osteolytic lesion in the proximal portion of the right tibia. An associated soft-tissue mass caused a medial deformity of the bone. A musculoskeletal survey revealed no additional lesions. A thoracic radiograph and an ultrasonographic study of the abdomen and pelvis revealed no abnormalities. A long leg cast was applied, and the infant was transferred to this hospital at 11 days of age.

The boy received breast milk every two hours during the day and every four hours at night. He nursed well and gained weight. He wet eight or more diapers daily and produced soft, yellow-brown stools once or twice daily. There was no history of fever, chills, rash, lethargy, irritability, diarrhea, vomiting, or difficulty with feeding or urination. There was no family history of endocrine or metabolic disease, bone tumors, childhood tumors, or childhood autoimmune disease.

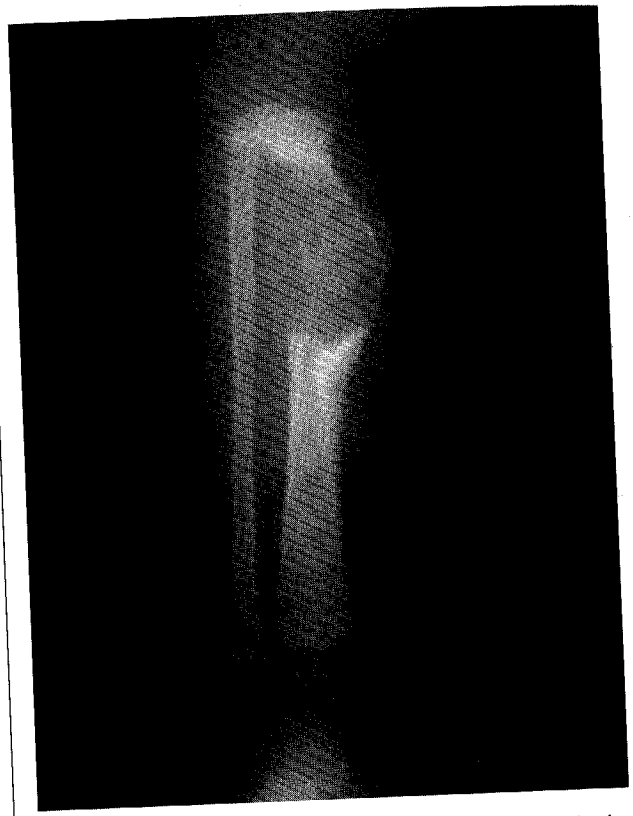

Figure 1. Radiograph Showing an Expansile Lytic Lesion in the Proximal Portion of the Right Tibia.

The temperature was 36.8°C, the pulse was 120, and the respirations were 34. The weight was 3680 g. The oxygen saturation was 98 percent while the boy was breathing oxygen at a rate of 2 liters per minute by the blow-by technique.

The physical examination showed no abnormalities except for the presence of a firm, raised mass in the proximal portion of the right lower leg; there was no local erythema or warmth as evidence of skin trauma. The legs were approximately equal in length. The urine was normal. The levels of urea nitrogen, creatinine, triglycerides, magnesium, aspartate aminotransferase, alanine aminotransferase, creatine kinase, and alkaline phosphatase were normal, as was the osmolality. The results of other laboratory tests are shown in Tables 1 and 2.

A magnetic resonance imaging (MRI) examination of the right leg (Fig. 2) showed an eccentric mass, 1.5 by 2.0 cm, in the proximal metaphysis of the tibia; the mass expanded the medial cortex of the bone and was accompanied by an overlying periosteal re-

TABLE 1. HEMATOLOGIC LABORATORY VALUES.

VARIABLE	VALUE
Hematocrit (%)	47.4
Reticulocyte count (%)	2.1
White-cell count (per mm³)	9,300
Differential count (%)	
Neutrophils	32
Lymphocytes	52
Monocytes	11
Eosinophils	3
Basophils	2
Platelet count (per mm³)	347,000

TABLE 2. BLOOD CHEMICAL AND ENZYME VALUES.*

VARIABLE	VALUE
Uric acid (mg/dl)	2.2
Calcium (mg/dl)	10.6
Phosphorus (mg/dl)	6.3
Protein (g/dl)	
Total	5.1
Albumin	3.0
Globulin	2.1
Sodium (mmol/liter)	139
Potassium (mmol/liter)	5.2
Chloride (mmol/liter)	103
Carbon dioxide (mmol/liter)	28.7
Lactate dehydrogenase (U/liter)	379

*To convert the value for uric acid to millimoles per liter, multiply by 59.48. To convert the value for calcium to millimoles per liter, multiply by 0.250. To convert the value for phosphorus to millimoles per liter, multiply by 0.3229.

action. The mass was isointense on T_1-weighted images and hyperintense on T_2-weighted images and was minimally enhanced after the administration of gadolinium; there was hyperintensity and enhancement in the surrounding soft tissue on the T_2-weighted images. The knee and ankle appeared normal. An MRI study of the abdomen revealed no abnormalities. A computed tomography (CT)–guided needle biopsy yielded nodular aggregates of hematopoietic marrow surrounded by reactive fibrosis with overlying periosteal formation of new bone. Special staining of the biopsy specimen ruled out a diagnosis of Langerhans'-cell histiocytosis and the presence of microorganisms, including acid-fast bacilli.

A diagnostic procedure was performed.

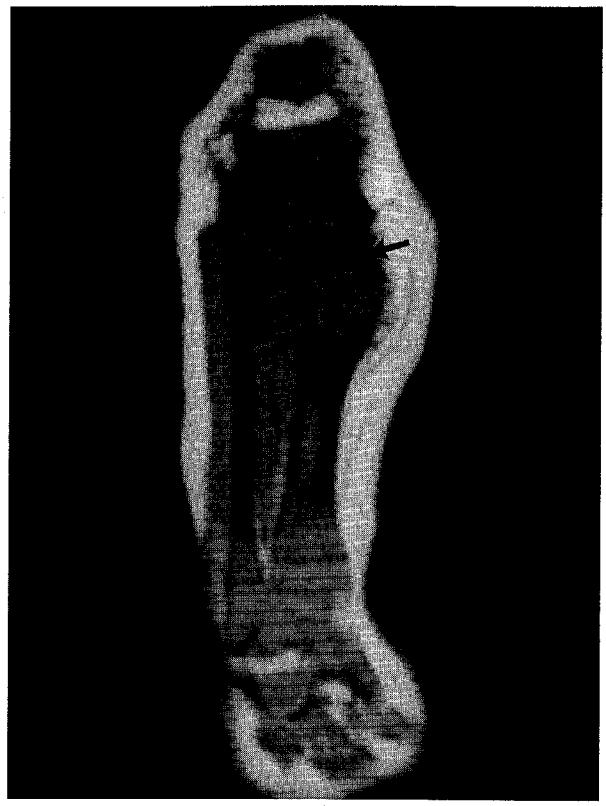

Figure 2. MRI Scan Showing a Mass (Arrow) with a Nonspecific Signal Extending from the Proximal Portion of the Right Tibia into the Soft Tissues.

DIFFERENTIAL DIAGNOSIS

DR. JOHN E. READY*: May we review the radiographic findings?

DR. ROBERT T. BRAMSON: A plain radiograph (Fig. 1) reveals a lytic lesion in the proximal portion of the right tibia. The MRI scan (Fig. 2) shows the lesion and a soft-tissue mass that extends out of the medial side of the proximal tibia. The various signal intensities described in the case record are nonspecific and do not provide a diagnostic clue.

DR. READY: This 11-day-old boy presented with an osteolytic lesion in the proximal portion of the right tibia. The differential diagnosis includes traumatic lesions, infections, metabolic disturbances, and neoplasms.

Trauma can be ruled out by the history of an uncomplicated vaginal delivery and the presence of the lesion at birth. Infection with subsequent osteomyelitis is very unlikely, since there were no clinical manifestations of an infection. The patient had no fever, and there was no warmth or erythema over the mass; the white-cell count was not elevated, and the differ-

*Department of Orthopedic Surgery, Brigham and Women's Hospital; clinical instructor in orthopedic surgery, Harvard Medical School — both in Boston.

ential count was normal. Metabolic diseases or disturbances usually result in multiple abnormalities of the bones or growth disturbances of the skeleton; this patient's lesion, however, was solitary, so it is unlikely that he had any type of generalized metabolic disorder.

Bone tumors can be benign or malignant and, if malignant, can be either primary or secondary. Cancer is rare in the first year of life, with a prevalence of 218.4 cases per million infants, although it appears to be increasing.[1,2] The most common form of infantile cancer is neuroblastoma, which accounts for one third to one half of all cases. This boy's lesion does not resemble a metastatic neuroblastoma, which usually has a permeative appearance on radiographic images, and there is no evidence of a primary neuroblastoma on the ultrasonographic study of the abdomen and pelvis or on the MRI study of the abdomen.

Other forms of cancer to consider in an infant are (in order of frequency) malignant tumors of the central nervous system, leukemia, retinoblastoma, malignant germ-cell tumors, sarcomas, and malignant hepatic tumors. Because of the location of the mass in this infant, sarcomas must be considered, but this type of tumor accounts for only 5 percent of all cancers. Bone sarcomas, such as Ewing's sarcoma and osteosarcoma, are rare in infants; they are more common in adults during the second and third decades of life. Ewing's sarcoma usually occurs in flat bones or in the diaphysis of long bones, not in the metaphysis, where this patient's lesion was located, and on radiographic images it often has a permeative appearance. Osteosarcoma occurs in the metaphysis of long bones, most commonly near the knee. However, it usually causes an osteoblastic response and a large, adjacent, soft-tissue mass. Congenital fibrosarcoma, which is rare in infants, is usually manifested as a soft-tissue tumor; presentation as a lytic lesion of bone would be highly unusual. Although malignant melanoma can be transmitted across the placenta,[1,2] metastasis of a maternal tumor to the fetus is very rare.

The differential diagnosis of benign neoplasms and tumor-like lesions of the proximal tibia in an infant includes Langerhans'-cell histiocytosis, solitary congenital fibromatosis, nonossifying fibroma, ossifying fibroma, and fibrous dysplasia.

The CT-guided needle biopsy in this infant was nondiagnostic, since the specimen was obtained from the edge of the lesion and not the mass itself. Langerhans'-cell histiocytosis can occur in children of any age; the solitary form, eosinophilic granuloma, is usually found in children over two years of age. In an infant, the disorder is usually characterized by multiple lesions and the disseminated form, known as Letterer–Siwe disease.[3] This disorder is fatal in infants, and the lesions can mimic almost any type of neoplasm.

The history of this patient's lesion points to a congenital process, possibly congenital fibromatosis (also called infantile myofibromatosis). Although a case similar to the one under discussion has been reported in a six-day-old infant, less than 10 percent of cases of this disorder involve solitary lesions of bone. Most of the cases are characterized by multiple, nodular lesions of the skin, subcutaneous tissues, soft tissues, bone, and viscera.[3,4]

Nonossifying fibroma is a benign bone lesion that is usually eccentric and that can cause a deviation of the cortex of bone, but it usually does not result in a soft-tissue mass of the size seen in this case. Ossifying fibroma (also called osteofibrous dysplasia) occurs almost exclusively in persons under 20 years of age and usually occurs in those under 10 years of age. Radiographic examination typically reveals a lytic lesion with sclerotic areas and a bowing deformity of the tibia.[5,6] The tibia and the fibula are the most commonly affected bones. The lesion is often intracortical, with intramedullary extension.

Fibrous dysplasia, which occurs only rarely in infants, often affects the ribs, tibia, femur, mandible, or maxilla. Persons with this condition often present with multiple lesions in the skeleton, which may result in bony deformities.[4] The lesions can expand the bone, and treatment is usually necessary to prevent their progression or a pathologic fracture. In addition, injury to the affected area may cause a fracture that results in subsequent swelling and deformity. Polyostotic fibrous dysplasia (the McCune–Albright syndrome) may be associated with endocrine dysfunction, such as precocious puberty, and with cutaneous pigmentation.

I believe that this patient has a benign lesion of the proximal tibia, such as fibrous dysplasia or osteofibrous dysplasia. I base this diagnosis on the solitary nature of the mass and the absence of evidence of trauma or a metabolic or infectious cause. Since osteofibrous dysplasia is usually located in the anterior portion of the tibia and is associated with considerable deformity, I favor fibrous dysplasia as the cause of the concentric expansion of the cortical bone.

Since no abnormalities were seen in the specimen from the CT-guided needle biopsy, I would proceed to an open surgical biopsy to make the diagnosis.

DR. FRANCIS J. HORNICEK, JR.: Our initial impression was that the lesion was benign. After we obtained the imaging studies of the abdomen and pelvis, we ruled out the possibility of a neuroblastoma that had metastasized to the tibia. The radiographic appearance was not that of a malignant bone tumor. Also, the child was young for Ewing's sarcoma or an osteosarcoma. We favored a benign process such as eosinophilic granuloma or a benign fibrous lesion. Of the benign fibrous lesions, fibrous dysplasia was highest on our list of diagnoses, but we were aware that if this diagnosis was correct, the case involved one of the youngest patients yet described to have it, and it could have manifested itself in utero.

We performed an incisional biopsy. After an intraoperative diagnosis was made on the basis of examination of a frozen section, we cleared the cavity of the lesion with a curet and applied a long leg cast.

CLINICAL DIAGNOSIS

Fibrous dysplasia.

DR. JOHN E. READY'S DIAGNOSIS

Fibrous dysplasia.

PATHOLOGICAL DISCUSSION

DR. SUZANNE B. KEEL: Microscopical examination of the specimen showed sheets of plump and spindle-shaped cells haphazardly present among scattered bundles of collagen (Fig. 3). In some areas, the spindle cells were arranged in a storiform pattern. Small trabeculae of woven bone, which lacked the osteoblastic rimming characteristic of reactive woven bone, were present on the fibrous background (Fig. 4). No cytologic atypia was present in the fibrous or osseous component. The diagnosis was fibrous dysplasia.

Fibrous dysplasia was described in the late 1930s by Albright and colleagues[7] and Lichtenstein.[8] Seventy to 80 percent of cases are known to be monostotic, but the proportion may actually be higher, because many patients are asymptomatic.[9] Fibrous dysplasia is more common in females than in males, and most patients with this condition are in their 20s or 30s; in 18 percent of the cases, the lesions arise in the tibia.[9] Fibrous dysplasia may be a component of Mazabraud's syndrome (fibrous dysplasia and intramuscular myxomas) as well as the McCune–Albright syndrome, but this patient does not have evidence of either of these disorders.[8] Fibrous dysplasia accounts for only 5 percent of bone lesions in children in the first decade of life, and is very rare in neonates.[10] Two siblings have been described with monostotic fibrous dysplasia of the jaw, diagnosed at 3 months and 12 days of age.[10] At one institution, only 6.5 percent of patients with fibrous dysplasia were under 10 years of age.[11] More common bone abnormalities in neonates include eosinophilic granuloma, infection, and metastatic neuroblastoma.[10]

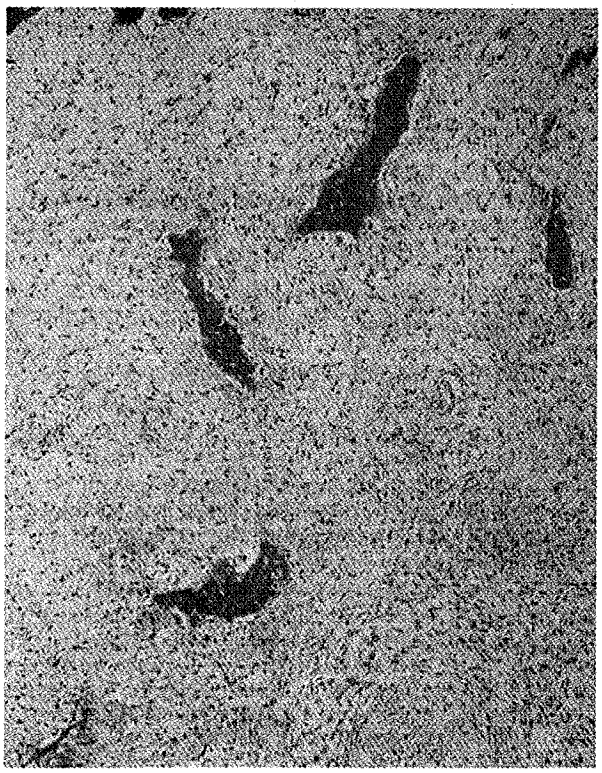

Figure 3. Irregular Trabeculae of Bone on a Background of Spindle Cells and Collagen (Hematoxylin and Eosin, ×40).

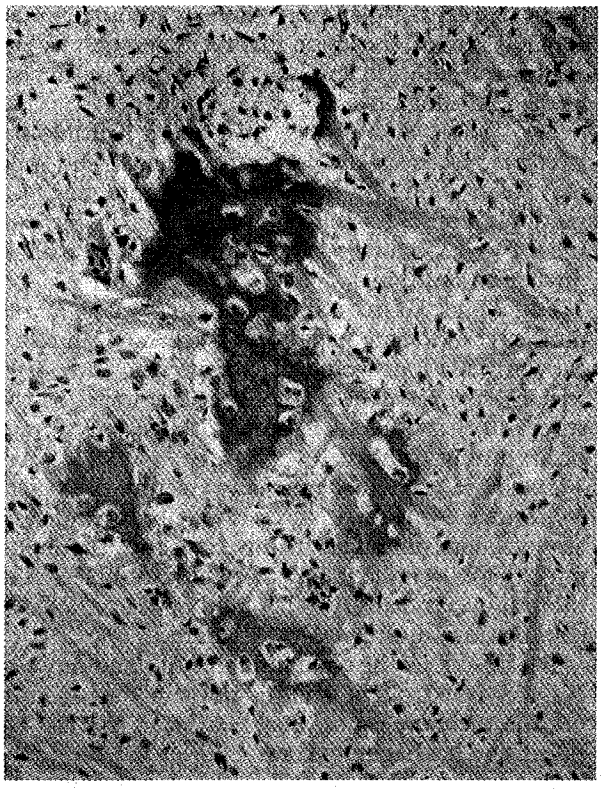

Figure 4. Woven Trabeculae of Bone Lacking Prominent Osteoblastic Rimming (Hematoxylin and Eosin, ×120).

DR. EUGENE J. MARK: What is the most common site of fibrous dysplasia?

DR. KEEL: The femur is one of the most common sites; in children, ribs and facial bones are often involved.

DR. READY: Why was a graft not performed?

DR. HORNICEK: We were confident that the potential for bone formation would be adequate to fill the cavity in a child this young. One problem with fi-

brous dysplasia is that even when an autograft or an allograft is used, the lesion may recur and destroy the graft. In an adult, an autograft is destroyed much faster than an allograft.

DR. KEITH P. MANKIN: Two and a half months after the resection, the cast was removed. The child now wears a long leg brace and undergoes range-of-motion exercises for the knee and the ankle. He uses the leg well spontaneously, with no apparent pain or further symptoms.

DR. MARK: If an ultrasonographic study of the mother's abdomen had been performed and had shown the lesion, would it have affected the obstetrician's management of the case? I am also a little surprised that a fracture through the lesion did not occur during delivery.

DR. MANKIN: I believe that a fracture did occur. More than 95 percent of cases of fibrous dysplasia are incidental findings. In this case, too, the lesion might have been silent, except that it was subjected to the trauma of delivery. The child appeared to have pain because the cortex had fractured.

DR. MARK: Is the child now able to stand or walk?

DR. MANKIN: The child is now only six months old and therefore is not yet able to stand or walk. He sits up and has begun to crawl. He will be wearing the long brace on his leg until the healing is complete. Other lesions may appear in the future. We plan to obtain another bone scan when the child is one year of age. We do not want to obtain it sooner because it is difficult to interpret bone scans in very young children.

ANATOMICAL DIAGNOSIS

Fibrous dysplasia.

REFERENCES

1. Isaacs H Jr. Tumors of the fetus and newborn. Philadelphia: W.B. Saunders, 1997.
2. *Idem.* Tumors of the newborn and infant. St. Louis: Mosby–Year Book, 1991.
3. Schaffzin EA, Chung SM, Kaye R. Congenital generalized fibromatosis with complete spontaneous regression: a case report. J Bone Joint Surg Am 1972;54:657-62.
4. Huvos AG. Bone tumors: diagnosis, treatment and prognosis. 2nd ed. Philadelphia: W.B. Saunders, 1991.
5. Smith NM, Byard RW, Foster B, Morris L, Clark B, Bourne AJ. Congenital ossifying fibroma (osteofibrous dysplasia) of the tibia — a case report. Pediatr Radiol 1991;21:449-51.
6. Sweet DE, Vinh TN, Devaney K. Cortical osteofibrous dysplasia of long bone and its relationship to adamantinoma: a clinicopathologic study of 30 cases. Am J Surg Pathol 1992;16:282-90.
7. Albright F, Butler AM, Hampton AO, Smith P. Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction, with precocious puberty in females: report of five cases. N Engl J Med 1937;216:727-46.
8. Lichtenstein L. Polyostotic fibrous dysplasia. Arch Surg 1938;36:874-98.
9. El Deeb M, Waite DE, Gorlin RJ. Congenital monostotic fibrous dysplasia — a new possibly autosomal recessive disorder. J Oral Surg 1979;37:520-5.
10. Senac MO Jr, Isaacs H, Gwinn JL. Primary lesions of bone in the 1st decade of life: retrospective survey of biopsy results. Radiology 1986;160:491-5.
11. Unni KK. Conditions that simulate bone neoplasms. In: Dahlin DC, ed. Bone tumors: general aspects and data on 11,087 cases. Philadelphia: Lippincott-Raven, 1996:367-76.